Ehrlichiosis

Section 1: ABOUT THE DISEASE

A. Etiologic Agent

Human granulocytic ehrlichiosis (HGE), or human granulocytotropic anaplasmosis, is a bacterial infection caused by *Anaplasma phagocytophilum* (formerly *Ehrlichia phagocytophila*). Human monocytic ehrlichiosis (HME) is caused by the bacterium *Ehrlichia chaffeensis*. The etiologic agents are rickettsiae and intracellular pathogens.

B. Clinical Description

The HGE and HME agents infect different white blood cells, but the signs, symptoms, and clinical courses of the two diseases are similar. Both cause sudden illness, with fever being the predominant sign. The clinical illness is similar to the early phase of Rocky Mountain spotted fever (RMSF), although patients more often have low white blood cell counts and less often develop rash. In addition to fever, patients may have headache, malaise, chills, muscle and joint aches, nausea, vomiting, and loss of appetite. Patients with HGE rarely have a rash, while about 40% with HME have a rash. Many people with HGE or HME may be asymptomatic or may have a very mild, self-limited illness. Treatment for both infections is antibiotics. Response to treatment is usually apparent within 24–48 hours.

Severe complications are associated with delayed treatment, older age, or with the case being immunocompromised or having diabetes. These complications may affect the lungs, bone marrow, brain, meninges (linings of the brain and spinal cord), kidneys, and blood. Fatal infections have been reported. Coinfections with other tickborne agents, such as the agents of Lyme disease and babesiosis, may complicate the clinical picture.

C. Vectors and Reservoirs

The vector of HGE is the deer tick, *Ixodes scapularis,* which is the same tick associated with Lyme disease and babesiosis. Deer ticks may be co-infected with and capable of transmitting more than one disease agent at the same time. Deer, elk, and wild rodents are likely reservoirs for HGE.

The primary vector of HME is the lone star tick, *Amblyoma americanum*. This tick is named for the prominent white spot or "star" on the back of the adult female. The lone star tick is predominantly found in the southeastern U.S. Lone star ticks infected with *E. chaffeensis* have been found in Connecticut and Rhode Island. Lone star ticks are not established in Massachusetts; however, there have been sporadic reports of lone star ticks found on Cape Cod. White-tailed deer are a major host of lone star ticks and appear to represent a natural reservoir for *E. chaffeensis.* Another important reservoir appears to be dogs.

D. Modes of Transmission

A. phagocytophilum, the agent responsible for HGE, is transmitted through the bite of an infected deer tick. *E. chaffeensis*, the agent responsible for HME, is transmitted through the bite of an infected lone star tick. Limited data suggest that the longer an infected tick remains attached, the higher the likelihood of successful transmission of *A. phagocytophilum* or *E. chaffeensis*. Since tick bites are often painless and may occur on parts of the body that are difficult to observe, cases of HGE and HME may have no known history of tick bite.

E. Incubation Period

The period between exposure to infection and the first symptoms of HME or HGE ranges from 7–14 days.

F. Period of Communicability or Infectious Period

HGE and HME are not communicable from person to person.

G. Epidemiology

In the U.S., HGE is most often reported in the northeastern and upper-midwestern states. HME is most often reported in the southeastern and southcentral states, reflecting the range of its tick vector. Ehrlichiosis was only recently added to the list of reportable diseases in Massachusetts (in 2003). Though surveillance data are limited, it appears the greatest risk of HGE in Massachusetts occurs along the southeastern coast and islands, particularly on Nantucket. However, as Lyme disease has spread throughout Massachusetts, it is likely that HGE will also spread throughout the state. The majority of HGE cases occur from June through August. Due to the limited number of cases reported, knowledge regarding the epidemiology of HME in Massachusetts is incomplete.

H. Bioterrorist Potential

This pathogen is not considered to be of risk for use in bioterrorism.

Section 2:
REPORTING CRITERIA AND LABORATORY TESTING

A. What to Report to the Massachusetts Department of Public Health (MDPH)

Report any clinically suspect case with supportive laboratory results.

Note: See Section 3C for information on how to report a case.

B. Laboratory Testing Services Available

Although the MDPH State Laboratory Institute (SLI) does not provide testing services for *Ehrlichia* at the time of this printing, development and evaluation of serological assays are in progress. At present, the SLI Viral Serology Laboratory can forward serum specimens to the Centers for Disease Control and Prevention (CDC) for testing. A complete case history should be included with each specimen.

For additional information on specimen submission and test availability, contact the SLI Viral Serology Laboratory at (617) 983-6396.

Note: The SLI does not provide services for tick identification or testing of ticks. See Section 4C for further information.

Section 3:

REPORTING RESPONSIBILITIES AND CASE INVESTIGATION

A. Purpose of Surveillance and Reporting

- To measure the prevalence of HGE and HME in Massachusetts.
- To identify where HGE and HME occur in Massachusetts.
- To focus prevention education.
- To target tick control measures.

B. Laboratory and Health Care Provider Reporting Requirements

Ehrlichiosis is reportable to the local board of health (LBOH). The MDPH requests that health care providers immediately report to the LBOH in the community where the case is diagnosed, all confirmed or suspect cases of ehrlichiosis, as defined by the reporting criteria in Section 2A.

Laboratories performing examinations on any specimens derived from Massachusetts residents that yield evidence of ehrlichiosis infection shall report such evidence of infection directly to the MDPH within 24 hours.

C. Local Board of Health (LBOH) Reporting and Follow-Up Responsibilities

Reporting Requirements

MDPH regulations (*105 CMR 300.000*) stipulate that ehrlichiosis is reportable to the LBOH and that each LBOH must report any case of ehrlichiosis or suspect case of ehrlichiosis, as defined by the reporting criteria in Section 2A. Cases should be reported to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS) using an official MDPH *Ehrlichiosis Case Report Form* (found at the end of this chapter). Refer to the *Local Board of Health Timeline* at the end of this manual's *Introduction* section for information on prioritization and timeliness requirements of reporting and case investigation.

Case Investigation

1. It is requested that LBOH complete a MDPH *Ehrlichiosis Case Report Form* (found at the end of this chapter) by interviewing the case and others who may be able to provide pertinent information. Much of the information required on the form can be obtained from the case's health care provider or from the medical record.
2. Use the following guidelines to assist in completing the case report form:
   a. Demographic information: Accurately record the demographic information.
   b. Clinical information: Accurately record clinical information including whether the case was hospitalized (and associated dates), date of symptom onset, symptoms, treatment information, health care provider information, and outcome of disease (e.g., recovered, died).
   c. Laboratory information: Check off all appropriate tests performed, and attach a copy of any laboratory results. Also note if the case was tested for other tickborne diseases, such as Lyme disease or babesiosis. Please refer to other chapters of this manual and complete the appropriate forms if the case tests positive for other diseases.

d. Exposure information: Use the incubation period range for HME or HGE (1–2 weeks). Specifically, focus on the period beginning a minimum of one week prior to the case's onset date back to no more than two weeks before onset for the following exposures:

   i. Tick bite history: Determine if the case was bitten by a tick. If yes, record information about the duration of tick attachment, date(s), and geographic location(s) where bites occurred.

   ii. Travel history: Determine the geographic area(s) of travel, including known areas of high risk, such as Cape Cod, Martha's Vineyard, and Nantucket.

e. If you have made several attempts to obtain case information but have been unsuccessful (e.g., the case or health care provider does not return your calls or respond to a letter, or the case refuses to divulge information or is too ill to be interviewed), please fill out the form with as much information as you have gathered. Please note on the form the reason(s) why it could not be filled out completely.

3. After completing the form, attach laboratory report(s) and fax or mail (in an envelope marked "Confidential") to ISIS. The confidential fax number is (617) 983-6813. Call ISIS at (617) 983-6801 to confirm receipt of your fax. The mailing address is:

MDPH, Office of Integrated Surveillance and Informatics Services (ISIS)
305 South Street, 5th Floor
Jamaica Plain, MA 02130
Fax: (617) 983-6813

4. Institution of disease control measures is an integral part of case investigation. It is the responsibility of the LBOH to understand, and if necessary, institute the control guidelines listed in Section 4.

Section 4:

CONTROLLING FURTHER SPREAD

A. Isolation and Quarantine Requirements *(105 CMR 300.200)*

None.

B. Protection of Contacts of a Case

None.

C. Managing Special Situations

Response to a Tick Bite

The longer a tick remains attached to the body, the higher the likelihood of disease transmission. Whenever an attached tick is removed from the body, one should monitor one's health for the appearance of rash, fever, or flu-like symptoms, and immediately seek the advice of a health care provider should any symptoms occur. It may be helpful to save the tick after removal for two reasons: 1) if the person who was bitten goes on to develop signs or symptoms such as fever,

flu-like symptoms, or a rash, it may be helpful for the physician to know the type of tick; and 2) depending on the circumstances of the bite (i.e., when a person was bitten, the type of tick, how long it was attached), a physician may choose to treat the person who was bitten. The tick may be kept either securely sealed within a small plastic bag or attached, with clear tape, to a piece of paper. For individuals who do not wish to keep the tick, it can be either drowned in rubbing alcohol or flushed down the toilet.

The MDPH does not provide tick identification or tick testing services. A listing of agencies that provide these services for a fee is available on the MDPH website at www.mass.gov/dph/cdc/epii/lyme/lymehp.htm.

If someone chooses to have the tick tested, the following information should be taken into account:

- Tests performed on ticks are not perfect, and they do not test for all infections that ticks may carry. Therefore, even with a negative result, people should still monitor for the appearance of rash, fever, or other unusual symptoms and immediately seek the advice of a health care provider should any symptoms occur.
- If someone has been infected by a tick bite, symptoms may begin to occur even before the results of tick testing are available. People should not wait for tick testing results before seeking medical advice should any symptoms develop.
- A positive test on a tick is not an automatic indication that treatment is needed. A positive test indicates that the tick was infected but not that the tick was successful in spreading the infection to the person bitten. The longer a tick is attached, the greater the chance that it will spread infection. Positive test results should be discussed with a health care provider.

D. Preventive Measures

Environmental Measures

Prevention of ehrlichiosis involves making the yard less attractive to ticks or their preferred hosts, the white-footed mouse (*Peromyscus leucopus*) and the while-tailed deer (*Odocoileus virginianus*). Advise individuals to:

- Keep grass cut short.
- Remove leaf litter and brush from around the yard.
- Prune low lying bushes to let in more sunlight.
- Keep woodpiles and bird feeders off the ground and away from the home.
- Keep the plants around stone walls cut short.
- Use a three-foot wide woodchip, mulch, or gravel barrier where the lawn meets the woods, and remind children not to cross that barrier.
- Ask a landscaper or local nursery about plants to use in the yard that do not attract deer.
- Use deer fencing (for yards 15 acres or more).

If one chooses to use a pesticide to reduce the number of ticks on one's property, one should hire a licensed applicator experienced with tick control. A local landscaper or arborist may be a licensed applicator. In general, good tick control can be achieved with no more than two pesticide applications in any year. When selecting an applicator, ask if they will provide:

- A written pest control plan that includes information on the pesticide to be used.
- Information about non-chemical pest control alternatives.
- Signs to be posted around the property after the application.

Personal Preventive Measures/Education

There is no human vaccine for HGE or HME. If someone lives, works, or spends leisure time in an area likely to have ticks, they should be advised of the following:

- The single most important thing one can do to prevent a tickborne disease is to check oneself for ticks once a day. Favorite places ticks like to go on the body include areas between the toes, back of the knees, groin, armpits, neck, along the hairline, and behind the ears. Remember to check children and pets too. Promptly remove any attached tick using fine-point tweezers. The tick should not be squeezed or twisted but grasped close to the skin and pulled straight out using steady pressure.
- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light-colored shirts, and long pants tucked into socks.
- Talk to a veterinarian about the best ways to protect pets and livestock from ticks.
- Use repellents containing DEET (N,N-diethyl-m-toluamide), and choose a product that will provide sufficient protection for the amount of time spent outdoors. Product labels often indicate the length of time that someone can expect protection from a product. DEET is considered safe when used according to the manufacturer's directions. The efficacy of DEET levels off at a concentration of 30%, which is the highest concentration recommended for children and adults. DEET products should not be used on children <2 months of age. The following precautions should be observed when using DEET products:
  - Avoid using DEET products that combine the repellent with a sunscreen. Sunscreens may need to be reapplied too often, resulting in an over application of DEET.
  - Apply DEET on exposed skin, using only as much as needed.
  - Do not use DEET on the hands of young children, and avoid applying repellent to areas around the eyes and mouth.
  - Do not use DEET over cuts, wounds, or irritated skin.
  - Wash treated skin with soap and water after returning indoors, and wash treated clothing.
  - Avoid spraying DEET products in enclosed areas.
- Permethrin-containing products will kill mosquitoes and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing. Because permethrin binds very tightly to fabrics, once the fabric is dry, very little of the permethrin gets onto the skin.

ADDITIONAL INFORMATION

The following is the formal CDC surveillance case definition for ehrlichiosis. It is provided for your information only and should not affect the investigation or reporting of a case that fulfills the criteria in Section 2A of this chapter. (The CDC and the MDPH use the CDC case definitions to maintain uniform standards for national reporting.) For reporting to the MDPH, always use the criteria outlined in Section 2A.

Note: The most up-to-date CDC case definitions are available on the CDC website at www.cdc.gov/epo/dphsi/casedef/case_definitions.htm.

Case Classification

Probable	A case must be clinically compatible and must meet one of the following laboratory criteria: ◆ A single immunofluorescence antibody (IFA) serologic titer ≥64; or ◆ The identification of intracytoplasmic morulae in blood, bone marrow, or cerebrospinal fluid (CSF) white blood cells.
Confirmed	A case must be clinically compatible and must meet one of the following laboratory criteria: ◆ A four-fold or greater change in antibody titer to *Ehrlichia* sp. antigen by IFA test in acute- and convalescent-phase specimens, ideally taken ≥4 weeks apart. HME diagnosis requires *E. chaffeensis* and HGE currently requires *E. equi* or HGE–antigen; ◆ A positive polymerase chain reaction (PCR) assay. Distinct primers are used for the diagnosis of HGE and HME; or ◆ The identification of intractyoplasmic morulae in blood, bone marrow, or CSF white blood cells, and an IFA antibody titer ≥64.

REFERENCES

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FORMS & WORKSHEETS

Ehrlichiosis

Ehrlichiosis

LBOH Action Steps

This form does not need to be submitted to the MDPH with the case report form. It is for LBOH use and is meant as a quick-reference guide to ehrlichiosis case investigation activities.

LBOH staff should follow these steps when ehrlichiosis is suspected or confirmed in the community. For more detailed information, including disease epidemiology, reporting, case investigation, and follow-up, refer to the preceding chapter.

- ❑ Obtain copies of relevant laboratory reports.
- ❑ Fill out a MDPH *Ehrlichiosis Case Report Form* (attach laboratory results).
- ❑ Send the completed case report form (with laboratory results) to the MDPH Bureau of Communicable Disease Control, Office of Integrated Surveillance and Informatics Services (ISIS).